UHASSELT
KNOWLEDGE IN ACTION

# Faculteit Revalidatiewetenschappen

## master in de revalidatiewetenschappen en de kinesitherapie

***Masterthesis***

***Prognostic parameters of all-cause mortality in heart failure patients from ZOL Genk: a retrospective cohort study***

**Iris Ivens**
**Kathy Verreydt**
Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen

**PROMOTOR :**
Prof. dr. Dominique HANSEN

**COPROMOTOR :**
dr. Kenneth VERBOVEN

**2020**
**2021**

UHASSELT
KNOWLEDGE IN ACTION

**www.uhasselt.be**
Universiteit Hasselt
Campus Hasselt:
Martelarenlaan 42 | 3500 Hasselt
Campus Diepenbeek:
Agoralaan Gebouw D | 3590 Diepenbeek

# Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

***Masterthesis***

***Prognostic parameters of all-cause mortality in heart failure patients from ZOL Genk: a retrospective cohort study***

**Iris Ivens**
**Kathy Verreydt**

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen

**PROMOTOR :**
Prof. dr. Dominique HANSEN

**COPROMOTOR :**
dr. Kenneth VERBOVEN

**Acknowledgements**

We would like to thank Ziekenhuis Oost Limburg (ZOL) Genk and Prof. dr. Wilfried Mullens for their cooperation. Physiotherapists Lore Jennes and Mirte Stifter for their clinical expertise and consultations.
A special thanks goes out to the physiotherapists from the cardiac rehabilitation department for lending us a space to work and for motivating us.

We would like to thank the other students from our student research group: Femke Tielemans and Minneke Verbeeck for their cooperation in data-collection. It was a pleasure working with you.

Thank you Natalia Turri Da Silva for your interest in our study, your feedback and tips to improve our work.
Thank you Mathias Verreydt for your feedback on our statistical analysis and for proof reading this thesis.

Lastly, we would like to thank our promoter Prof. dr. Dominique Hansen and co-promoter dr. Kenneth Verboven for their expertise and accompaniment on this thesis.

Dalstraat 31 2222 Wiekevorst, 31/05/2021 K. V.

Leuvensebaan 234 3040 Sint-Agatha-Rode, 31/05/2021 I. I.

**Research context**

Heart failure is currently still one of the leading causes of hospital admission worldwide and is an important cause of death (Ponikowski et al., 2014). In Belgium, 15.643 new patients are diagnosed every year. Due to the unfavorable prognosis of the disease, a lot of patients need to be rehospitalized one year after their initial admission (Devroey & Van Casteren, 2010). These admissions generate a high cost for Belgian health care (Claes, Jacobs & Vijgen, 2008).

Several studies about predictive parameters for mortality have been done in Europe and other countries worldwide (Mosterd et al., 2007; Rahimi et al., 2014; Eschalier et al., 2015). Still, not a lot of this information has been confirmed for Belgium specifically. This information could be useful to doctors, clinicians, patients and scientists for more individualized therapy.

This master thesis belongs to the rehabilitation of internal diseases, more specifically cardiac diseases. Since we study physical therapy, we had a special interest in the current situation of rehabilitation in heart failure patients. Especially because in-hospital cardiac rehabilitation is associated with a reduction of mortality and rehospitalization (Scalvini et al., 2019).

This is a standalone project of UHasselt in collaboration with Ziekenhuis Oost Limburg (ZOL) Genk. A parallel study exists using the same study population with a different research question and outcomes. Students from both projects formed a student research group and will be referred to as such. Both studies are coordinated by Prof. dr. Dominique Hansen as promoter and dr. Kenneth Verboven as co-promoter.

Due to Covid-19, the original concept for this master thesis was changed from a prospective study to a retrospective observational cohort study. The student research group initiated this change and consulted promotor, co-promotor and researchers from ZOL Genk for retrospective options. New research topics were established after this consultation.

Finalization of the research question was done by the students for their own study.

Method of data collection was established and finalized by the student research group. Data extraction from patient files was done by the student research group in ZOL Genk.

Method of data analysis was chosen by students and approved by the promoter. The analysis and interpretation were done by the students.

This thesis was fully written by the students.

**Reference list**


- Mosterd, A.; Hoes, A. W (2007). *Clinical epidemiology of heart failure. Heart, 93(9), 1137–1146.* doi:10.1136/hrt.2003.025270
- Ponikowski, P., Voors, A. A., Anker, S. D., Bueno, H., Cleland, J. G., Coats, A. J., ... & Van Der Meer, P. (2016). 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *European heart journal*, *37*(27), 2129-2200.
- Devroey, D., & Van Casteren, V. (2010). The incidence and first-year mortality of heart failure in Belgium: a 2-year nationwide prospective registration. International journal of clinical practice, 64(3), 330-335.
- Claes, N., Jacobs, N., & Vijgen, J. (2008). Impact of heart failure on hospital activity and healthcare costs in Belgium. Journal of Medical Economics, 11(1), 71-79.
- Rahimi, K., Bennett, D., Conrad, N., Williams, T. M., Basu, J., Dwight, J., ... & MacMahon, S. (2014). Risk prediction in patients with heart failure: a systematic review and analysis. *JACC: Heart Failure*, *2*(5), 440-446.
- Eschalier, Romain; Chenaf, Chouki; Mulliez, Aurélien; Yalioua, Arab; Clerfond, Guillaume; Authier, Nicolas; Vorilhon, Charles; Citron, Bernard; Pereira, Bruno; Jean, Frédéric; Souteyrand, Géraud; Motreff, Pascal; Eschalier, Alain; Lusson, Jean-René (2015). *Impact of Clinical Characteristics and Management on the Prognosis of Unselected Heart Failure Patients. Cardiovascular Drugs and Therapy, 29(1), 89–98.* doi:10.1007/s10557-015-6572-y
- Scalvini, S., Grossetti, F., Paganoni, A. M., Teresa La Rovere, M., Pedretti, R. F., & Frigerio, M. (2019). Impact of in-hospital cardiac rehabilitation on mortality and readmissions in heart failure: A population study in Lombardy, Italy, from 2005 to 2012. *European journal of preventive cardiology*, *26*(8), 808-817.

# 1. Abstract

**Background:** In Belgium, 15.643 people are diagnosed with heart failure every year. Since heart failure is one of the leading causes of mortality, a clear vision on predictive parameters could be useful to optimize treatment and minimize mortality.

**Method:** Data was extracted from patient files in ZOL Genk. Sex, age, weight, length, BMI, systolic blood pressure, diastolic blood pressure, HbA1c, HDL, LDL, triglycerides, NT-proBNP, diastolic dysfunction, NYHA class, smoking habits, comorbidities, cardiac history, presence of a device and in-hospital rehabilitation were collected and analyzed for predictive value of mortality one year after hospitalization.

**Results:** Through univariate logistic regression, age, diastolic BP, systolic BP, diastolic dysfunction, weight, BMI and HFrEF were found as significant independent predictive parameters for mortality. In a multivariate regression model only diastolic BP remained a significant parameter.

**Discussion and conclusion:** Most significant parameters from the study were not the most measured parameters at ZOL Genk. Future research on in-hospital rehabilitation is recommended to further establish its predictive value.

**Purpose of this study:** The aim of this study was to verify the predictive value of established predictors, and in-hospital rehabilitation specifically, on mortality in ZOL Genk. A secondary aim of the study was to evaluate if these parameters are measured the most often in ZOL Genk.

**Operationalization research question:** Which parameters found in patient files predict mortality in heart failure patients and are these commonly present in patient files at ZOL?

**Most important keywords:** Heart failure, Prognosis, Mortality, Cardiac rehabilitation, In-hospital rehabilitation, Retrospective

## 2. Introduction

Heart failure (HF) is defined as a clinical syndrome with typical signs and symptoms caused by a structural and/or functional cardiac abnormality, resulting in a diminished cardiac output and/or increased cardiovascular pressure (Ponikowski et al., 2016). A wide variety of risk factors can increase the incidence of HF such as increased age, BMI, cardiac history, use of medication, smoking habits, diabetes mellitus and renal function (Jacobs et al., 2017).

Worldwide, around 26 million people live with HF, of which 17-45% die within one year of hospital admission (Ponikowski et al., 2014). In Belgium, 15.643 new patients are diagnosed with HF every year. Although treatments for HF have strongly improved over the last few years, it is still one of the leading causes of hospital admission in elderly people and becomes one of the leading causes of morbidity and mortality (Devroey & Van Casteren, 2010). These hospitalizations are expensive to society. In 2008 Claes, Jacobs, and Vijgen wrote that 1.8% of the total in-hospital cost (€94.113.827) for Belgium goes to the primary diagnosis of heart failure, of which 67% is spent on hospitalizations.

In Western Europe, mortality after one year was estimated at 18.4% in hospitalized patients and 6.2% in ambulatory patients (Maggioni et al., 2013). According to Rahimi et al. (2014), the most important predictors of death in HF patients are age, renal function, blood pressure, blood sodium level, left ventricular ejection fraction, sex, brain natriuretic peptide level, New York Heart Association functional class, diabetes, weight or body mass index, and exercise capacity. A multidisciplinary approach is recommended to reduce the risk of hospitalization and mortality. Regular aerobic exercises should be a part of this approach and physiotherapists should be included in the multidisciplinary team (Ponikowski et al., 2016).

According to Scalvini et al. (2019), in-hospital cardiac rehabilitation is associated with a reduction in all-cause mortality and rehospitalization. Yet only 9% of HF patients in Belgium actually follow in-hospital cardiac rehabilitation (Pardaens, Marie Willems, Vande Kerckhove & De Sutter, 2015).

To our knowledge, there is not a lot of research available specifically for the Belgian HF population. Thus, the aim of this study was to verify the predictive value of established predictors of mortality of Belgian HF patients, specifically from ZOL Genk. Other parameters found in patient files were also examined to look for other potentially important predictive risk factors that might not have received a lot of attention in previous research. Specifically, the predictive value of in-hospital rehabilitation at ZOL Genk.

As a secondary aim, this study examined whether the most important predictors of mortality in HF patients were also the parameters which were most frequently collected at ZOL Genk. To complete the profile on ZOL Genk, the current situation on in-hospital cardiac rehabilitation was also explored.

## 3. Method

### 3.1 Study design

This was an observational cohort study with a retrospective design about HF patients at Ziekenhuis Oost Limburg (ZOL) Genk.

### 3.2 Participants

At ZOL Genk, a list was available of all patients diagnosed with HF according to ESC guidelines (Ponikowski et al., 2016). They were enrolled in the study when they were hospitalized for cardiac reasons in ZOL Genk between January 2015 and December 2019. All phenotypes of heart failure were included. Patients were followed up for one year (with a margin of three months) to gather information about rehabilitation and/or all-cause death one year after hospitalization.
Two exclusion criteria were used: 1) patients under the age of 18; 2) no cardiac hospitalization between 2015 and 2019.

Over a period of four weeks, during April 2021, as many patients as possible were included with a minimum of at least 200 patients.

The study was approved by BAREC, de Belgian Association of Research Ethics Committees. A final approval from the Clinical Trial Unit from ZOL Genk was received on 19/03/2021 with number: ctu2020131.

### 3.3 Procedure

The primary outcome measure was all-cause mortality as found in the patient files between the first cardiac hospitalization (between 2015 and 2019) and one year after. A margin of three months was used to define ‘one year’, creating a range between nine and fifteen months.

As a secondary outcome measure, information about measured data at ZOL Genk was collected. A small profile on the amount of collected data at ZOL Genk was made. Emphasis was placed on the percentage of patients following in-hospital rehabilitation and their outcome.

The collected data from the patient files at first cardiac hospitalization between 2015 and 2019 were the following: sex, age, weight, length, BMI (body mass index), systolic blood pressure, diastolic blood pressure, HbA1c (hemoglobin A1c), HDL (High-density-lipoprotein), LDL (Low-density-lipoprotein), triglycerides, NT-proBNP (N-terminal pro b-type natriuretic peptide), diastolic dysfunction, NYHA class (New York Heart association classification), smoking habits, comorbidities [DMT2 (diabetes mellitus type 2), COPD (chronic obstructive pulmonary disease), renal insufficiency, cancer], cardiac history, presence of a device and whether or not the patient followed in-hospital rehabilitation within one year of hospitalization. LVEF (left ventricular ejection fraction) was collected through available percentages in the patient files. These percentages were converted to categories (HFpEF, HFmrEF, HFrEF) according to the European Guidelines (Ponikowski et al., 2016). All these parameters were used to predict mortality.

If a variable was not available at the date of hospitalization, it was recorded as 'not available' (an overview of the used parameters is available in table 1). Follow-up data about rehabilitation and death had to be available within one year and three months after the date of hospitalization. All data was gathered in a spreadsheet where only the patient file number was used for privacy reasons.

Nobody was excluded due to insufficient available data. No matter how many parameters were (un)available for a specific patient, everybody who did not meet exclusion criteria was included. Thus, a chart selection bias was avoided. Only data from the day of hospitalization was collected, data which was not available at the day of hospitalization but some weeks before or after were not collected to avoid an assumption bias.

All parameters and outcomes were collected through Hix © (ChipSoft B.V. 2021). Specific information about rehabilitation was double checked through CGM Oxygen © (CompuGroup Medical 2021), software used by physiotherapists.

### 3.4 In-Hospital Rehabilitation Protocol

The in-hospital rehabilitation was standardized and went as follows:

Every heart failure patient that was hospitalized at ZOL Genk, was informed about the option to rehabilitate at the rehabilitation center of the hospital, where they had three group sessions each week for a total of 45 sessions. During the first session, physical therapists executed a CPET and 1RM tests of the upper and lower extremities. If the patient recently received a CABG, pacemaker or other device, upper body testing and training was postponed until eight weeks after surgery. Each patient followed an individual rehabilitation plan based on the results of the tests, which was adjusted according to the progress of the patient. Each session consisted of cardiovascular- and strength exercises. Upper body strength training consisted of pull downs and triceps dips. Lower body strength training was executed by leg press. Strength training was set at 60% of 1RM, which was tested regularly. Strength testing and training was performed on Enraf-Nonius Compass® 530 machines and cardiovascular training on the Enraf-Nonius Kardiomed® 700 machines. Cardiovascular exercises were done on a stationary bike, arm bike, row machine, seated bike, treadmill, cross trainer or step for ten minutes each. As a variation of endurance training on the stationary bike, an interval training was given to some patients. The intensity of the cardiovascular training on the bike was set at the first ventilatory threshold approximately, determined by the patient's VO2max that was tested through CPET. After 45 sessions, patients could continue to rehabilitate in a maintenance group, where they still had two group sessions each week.

### 3.5 Data analysis

JMP® 15 Pro (Cary, NC, 1989-2019) was used for all statistical analysis. Significance levels were set at 99% ($p < 0.01$), 95% ($p < 0.05$) and 90% ($p < 0.10$). Through univariate regression models, independent significance levels were established for all parameters. Only available data for each parameter was used. Missing values were not used or imputed in univariate analysis.

All significant nominal parameters were analyzed for correlations. Correlations were estimated through restricted maximum likelihood (REML). Above 0.500 correlations were considered too high to be used together in a multivariate model. Only the most significant parameter was used.

Results from previous analyses were used to decide which parameters would be put together in a multivariate logistic regression model to investigate their predictability on mortality. All significant parameters were used together with NT-proBNP and rehabilitation values regardless of significance. In this multivariate model nominal missing values were estimated with an imputation model.

For each parameter, percentages were calculated to establish how often a specific parameter was measured in the average HF patient in ZOL Genk.

# 4. Results

## 4.1 Participants

A total of 366 patients (table 1) were included in the study analysis. All data was collected at the date of hospitalization. Only rehabilitation setting and mortality were followed up for one year after hospitalization. One outlier was discovered for NT-proBNP, this value was removed from the dataset. In table 2, missing values per parameter were shown.

## 4.2 Predictability of mortality

### 4.2.1 Univariate analysis

Univariate analysis shows seven parameters of significance (table 3). One parameter with 99% significance level (SL): diastolic BP; three with 95% SL: age, systolic BP & diastolic DF grade 3; and three with 90% SL: weight, BMI & HFrEF. These variables were able to independently predict mortality in patients with heart failure.

Systolic BP, Diastolic BP, BMI and weight show a negative estimate with a significant p-value. Meaning an increase in these parameters equals a decrease at the chance of dying in heart failure patients one year after hospitalization. Odds ratio for these parameters show the same trend. For example, patients whose BMI lowers with one kg/m2 equals a 5% higher chance of dying within one year after hospitalization.

Age, HFrEF and diastolic dysfunction grade 3 show a positive estimate with a significant p-value. Meaning, a decrease in these parameters will significantly decrease the chance of dying in heart failure patients one year after hospitalization. Odds ratio for these parameters show the same trend. For example, patients aging within one year gives them 3% more chance of dying within one year after hospitalization.

For univariate analysis none of the missing values were imputed.

#### 4.2.2 Correlations

In table 4 correlations between significant parameters from univariate analysis were shown. There is one very strong correlation between weight and BMI. An explanation for this connection can be found in the formula of BMI which includes weight. Another strong correlation exists between systolic and diastolic blood pressure. This relation was expected since both parameters measure blood pressure. Only the most significant parameter will be used in multivariate regression. Therefore, only weight and diastolic blood pressure will be used without BMI and systolic blood pressure.

#### 4.2.3 Multivariate analysis

Five significant parameters (age, BMI, diastolic BP, LVEF and diastolic dysfunction) were used together with control variables (sex and comorbidities) in a multivariate logistic regression model (table 5). Missing values for nominal parameters were imputed by multivariate normal imputation. One parameter remained significant (90% significance level) in this model. Diastolic BP showed a negative linear relation, meaning a decrease in diastolic BP results in a higher mortality rate.

### 4.3 Analysis of data-collection in ZOL Genk

#### 4.3.1 Comparison with study results

The results showed greatest significance (99% SL) in diastolic BP. When comparing this to the amount of data measured in ZOL Genk, it was not the most measured parameter. Diastolic BP was measured in 69.70% (figure 1) of the heart failure patients from this study. When comparing with the other nineteen parameters, nine parameters were measured more often and nine parameters were measured less often.

Three parameters were significant on a 95% SL in univariate analysis. The first one, age, was measured the most out of all parameters (100%). The second parameter, systolic BP, was measured just as often as diastolic BP (69.70%). As previously stated, nine parameters were measured more often and nine parameters were measured less often. The third parameter, diastolic dysfunction, was measured in 54.40% of the study population. Only three parameters were measured less often.

On a 90% SL, also three parameters were significant in univariate analysis. The first was weight, which was measured in 69.90% of the study population. Eight parameters were measured less often, eleven parameters were measured more often. The second parameter was BMI, which was measured in 67.20% of the study population. Seven parameters were measured less often and twelve parameters were measured more often. The third parameter was LVEF. This was measured in 76% of the study population. Twelve parameters were measured less and seven parameters were measured more often.

#### 4.3.2 In depth analysis of NT-proBNP

According to Spinar et al. (2019) NT-proBNP is an important parameter to predict prognosis in HF. Low levels are associated with excellent prognosis and high levels predict an unfavorable prognosis. Their article also concluded that the discriminatory value of a prediction model based on clinical parameters can be improved by taking NT-proBNP into consideration. Therefore NT-proBNP was included in the multivariate analysis regardless of the significance in the univariate analysis.

The mean percentage in this study increased between 2015 (15%) and 2018 (32%). There were only 26 patients from 2019 included and due to the low sample size for that year (< 30), it was not further explored.

#### 4.3.3 In depth analysis of rehabilitation

All parameters were analyzed with univariate regression for predictive value for in-hospital rehabilitation. In table 6, all significant parameters are shown.

The Belgian mean of in hospital rehabilitation is around 9% (Pardaens et al., 2015). The mean percentage in this study increased between 2016 (7.64%) and 2018 (13.64%). There were only 26 patients from 2019 included and due to the low sample size from that year (< 30), it was not further explored.

## 5. Discussion

### 5.1 Dataset

A strength of this study was that an assumption bias was avoided by only collecting data at the date of hospitalization. Also, a chart selection bias was avoided by including all patients no matter how little data was available.

In this dataset, a mortality percentage of 15.5% was found, which is lower than the mean mortality rate of 18.4% in Western Europe (Maggioni et al., 2013). Representation in this study might be too low or mortality in heart failure might still be decreasing. However, the possible underrepresentation might have affected the predictive values in a negative way.

Even though NT-proBNP is an important parameter to predict prognosis in HF (Spinar et al., 2019), it was only measured in 23% of the study population. This might be a reason NT-proBNP shows no significance in predicting mortality in this study. Every year the mean measured percentage of NT-proBNP increases at ZOL Genk. In 2019, the percentage also increased, but due to the low sample size of 2019 in this study, this measurement was not included in the analysis. We advise ZOL Genk to keep increasing the number of patients in which NT-proBNP is collected, and if possible, measure it in every HF patient.

NYHA class and HbaA1c were also measured in less than 50% of this study population, even though literature (Rahimi et al., 2014) states the importance of these parameters in predicting mortality in HF patients. Although this study did not find the same importance, we still recommend ZOL Genk to collect these parameters more often.

In this study, in-hospital rehabilitation was followed by only 11% of the patients. While this percentage is slightly higher than in the study of Pardaens et al. (2015), who found that 9% of Belgian HF patients followed in-hospital rehabilitation, it is still a small number of patients that do follow rehabilitation. Heart failure guidelines recommend physical rehabilitation as a priority intervention. In patient files it was clear that more than 11% followed in-hospital rehabilitation but a big part of the group started later than one year after their first hospitalization. Some possible reasons can be found specifically in ZOL Genk where cardiac rehabilitation was not recommended by cardiac specialists until 2015. Even now, only one physician recommends it for all his cardiac patients. Another more general reason is reevents. More patients might wait to follow rehabilitation because they do not think their condition is serious enough until a second event happens. Future research can confirm whether this is an important factor in their decision to start cardiac rehabilitation or not.

### 5.2 Results

Results from this study confirm only seven predictive parameters in univariate analysis. Other parameters (renal function, left ventricular ejection fraction, sex, brain natriuretic peptide level, New York Heart Association functional class, diabetes, and exercise capacity) were not significant even though Rahimi et al. (2014) showed that these were important significant predictive parameters for mortality in HF. The possible underrepresentation of mortality and the amounts of missing values from important parameters requires us to interpret results with caution.

In univariate analysis, a higher BMI score significantly predicted a lower mortality rate. This complex relationship was first described by (Horwich et al., 2001) and was later called the BMI or obesity paradox.

When looking at measured percentages of parameters it was clear that outcomes with “yes or no” have a 100% measurement. Sex and age also have a 100% measurement because in Belgium, it is required to identify yourself with legal documents when being hospitalized. Continuous or categorical parameters with more than 2 categories were measured less. Probably because they often require more specific imaging techniques and/or time to interpret.

### 5.3 Limitations

Data was collected through patient files at ZOL Genk. This was done by four students independently from each other. Collected data was not double checked. Guidelines on where to find measurements for each parameter were established. Questions regarding the data were discussed and a consensus was reached among all students. However, not all data was found in the same place in a patient file and none of the files were fully complete. Due to the complexity of the patients’ files, it is possible some information was overlooked or incorrectly transcribed. The same students both collected the data and assessed the outcomes, possibly creating an observation bias. A missing data in charts bias is possibly also present. Due to this bias, it is possible some results are over- or underestimated.

In this study, medication was not one of the variables because of the complexity in patient files.

The study population consisted only of patients from ZOL Genk. Even though we do not expect big differences between the populations of other Belgian hospitals, generalization for Belgium is limited and impossible worldwide without creating a generalization bias. Only 11% of our sample size followed cardiac rehabilitation at ZOL Genk, which makes it impossible to draw conclusions on whether cardiac rehabilitation would ensure a better outcome one year after first hospitalization or not.

### 5.4 Recommendations future research

For future research, a bigger sample size is recommended for more statistical power. With a prospective study design all parameters can be measured for the study population. We recommend using two groups: 1) heart failure patients following in-hospital rehabilitation and 2) heart failure patients without in-hospital rehabilitation. Through this design more specific attention can be given to the effects of cardiac rehabilitation and its predictive value.

Guidelines recommend this as a primary intervention yet only 11% of this study population underwent rehabilitation. However, patients might wait to follow rehabilitation because they do not think their condition is serious enough until a second event happens. More research should be done regarding these cognitions towards cardiac rehabilitation to understand the small rehabilitation percentage.

For ZOL Genk we recommend collecting the most important predictive parameters in all their HF patients. Especially BP, diastolic dysfunction, weight, BMI and LVEF should be measured in as many HF patients as possible.

## 6. Conclusion

There were seven parameters which predicted mortality in HF patients in univariate analysis: age, diastolic BP, systolic BP, diastolic dysfunction, weight, BMI and HFrEF. In a multivariate model, there was only one predictive parameter left: diastolic BP. The most significant parameters were not the ones that were most often collected at ZOL Genk. Only parameters that were easy to collect (age and sex) were always measured. Parameters that require more extensive research were less often collected (diastolic dysfunction grade, NT-proBNP and HbA1c). Despite recommendations of rehabilitation in the European guidelines, only 11% of the total study population followed in-hospital rehabilitation. More prospective research is recommended to investigate if in-hospital rehabilitation at ZOL Genk ensures a better prognosis for patients with HF.

## 7. Reference list


Claes, N., Jacobs, N., & Vijgen, J. (2008). Impact of heart failure on hospital activity and healthcare costs in Belgium. Journal of Medical Economics, 11(1), 71-79.

Devroey, D., & Van Casteren, V. (2010). The incidence and first-year mortality of heart failure in Belgium: a 2-year nationwide prospective registration. International journal of clinical practice, 64(3), 330-335.

Jacobs, L., Efremov, L., Ferreira, J. P., Thijs, L., Yang, W., Zhang, Z., … Poulter, N. (2017). Risk for Incident Heart Failure: A Subject-Level Meta-Analysis From the Heart “OMics” in AGEing (HOMAGE) Study. Journal of the American Heart Association, 6(5), 1–10. https://doi.org/10.1161/jaha.116.005231

Maggioni, A. P., Dahlström, U., Filippatos, G., Chioncel, O., Leiro, M. C., Drozdz, J., ... & Heart Failure Association of the European Society of Cardiology (HFA). (2013). EURObservational Research Programme: regional differences and 1-year follow-up results of the Heart Failure Pilot Survey (ESC-HF Pilot). *European journal of heart failure*, *15*(7), 808-817.

Pardaens, S., Marie Willems, A., Vande Kerckhove, B., & De Sutter, J. (2015). Participation in cardiac rehabilitation after hospitalisation for heart failure: A report from the BIO-HF registry. *Acta cardiologica*, *70*(2), 141-147.

Ponikowski, P., Anker, S. D., AlHabib, K. F., Cowie, M. R., Force, T. L., Hu, S., ... & Filippatos, G. (2014). Heart failure: preventing disease and death worldwide. *ESC heart failure*, *1*(1), 4-25.

Ponikowski, P., Voors, A. A., Anker, S. D., Bueno, H., Cleland, J. G., Coats, A. J., ... & Van Der Meer, P. (2016). 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. European heart journal, 37(27), 2129-2200.

Rahimi, K., Bennett, D., Conrad, N., Williams, T. M., Basu, J., Dwight, J., ... & MacMahon, S. (2014). Risk prediction in patients with heart failure: a systematic review and analysis. *JACC: Heart Failure*, *2*(5), 440-446.

Scalvini, S., Grossetti, F., Paganoni, A. M., Teresa La Rovere, M., Pedretti, R. F., & Frigerio, M. (2019). Impact of in-hospital cardiac rehabilitation on mortality and readmissions in heart failure: A population study in Lombardy, Italy, from 2005 to 2012. *European journal of preventive cardiology*, *26*(8), 808-817.

Spinar, J., Spinarova, L., Malek, F., Ludka, O., Krejci, J., Ostadal, P., ... & Parenica, J. (2019). Prognostic value of NT-proBNP added to clinical parameters to predict two-year prognosis of chronic heart failure patients with mid-range and reduced ejection fraction–A report from FAR NHL prospective registry. *PloS one*, *14*(3), e0214363.

Tamara B Horwich; Gregg C Fonarow; Michele A Hamilton; W.Robb MacLellan; Mary A Woo; Jan H Tillisch (2001). The relationship between obesity and mortality in patients with heart failure. , 38(3), 789–795. doi:10.1016/s0735-1097(01)01448-6

## 8. Appendix

**Table 1.**

*Heart failure patient characterization in ZOL Genk.*

| Parameter | n (%) | Mean (SD) |
|---|---|---|
| **Age (year)** | 366 (100) | 73 (10) |
| **Sex** | 366 (100) | - |
| Female | 125 (34) | - |
| Male | 241 (66) | - |
| **Weight (kg)** | 256 (70) | 81 (17) |
| **Length (cm)** | 253 (69) | 168 (11) |
| **BMI (kg/cm$^2$)** | 246 (67) | 28 (5) |
| **Systolic BP (mmHg)** | 255 (70) | 129 (25) |
| **Diastolic BP (mmHg)** | 255 (70) | 71 (16) |
| **HbA1c (mmol/mol)** | 157 (43) | 45 (13) |
| **HDL (mg/dL)** | 208 (57) | 46 (16) |
| **LDL (mg/dL)** | 204 (56) | 78 (36) |
| **Triglycerides (mg/dL)** | 214 (59) | 127 (83) |
| **NT-ProBNP (ng/L)** | 85 (23) | 4103 (5289) |
| **LVEF** | 278 (76) | - |
| HFpEF | 108 (29) | - |
| HFmrEF | 66 (18) | - |
| HFrEF | 104 (28) | - |
| **Diastolic dysfunction** | 167 (46) | - |
| 1 | 93 (25) | - |
| 2 | 58 (16) | - |
| 3 | 16 (4) | - |
| 4 | 0 (0) | - |
| **NYHA** | 45 (13) | - |
| I | 3 (1) | - |
| II | 16 (4) | - |
| III | 21 (6) | - |
| IV | 5 (1) | - |
| **In-hospital rehabilitation** | 366 (100) | - |
| Yes | 43 (12) | - |
| No | 323 (88) | - |
| **Smoking habits** | 348 (95) | - |
| Yes | 47 (13) | - |
| Stopped | 149 (41) | - |
| No | 152 (41) | - |
| **Diabetes type 2** | 366 (100) | - |
| Yes | 137 (37) | - |
| No | 229 (63) | - |
| **COPD** | 366 (100) | - |
| Yes | 86 (23) | - |
| No | 280 (77) | - |
| **Renal insufficiency** | 366 (100) | - |

| | | |
|---|---|---|
| Yes | 99 (27) | - |
| No | 267 (73) | - |
| **Cancer** | 366 (100) | - |
| Yes | 20 (5) | - |
| No | 346 (95) | - |
| **Cardiac history** | 366 (100) | - |
| Yes | 351 (96) | - |
| No | 15 (4) | - |
| **Device** | 366 (100) | - |
| Yes | 192 (52) | - |
| No | 174 (48) | - |

**Legend:** Amounts with percentages of patients per parameter and mean score for continuous parameters with standard deviation.
**Abbreviation:** Amounts of patients (n), standard deviation (SD), body mass index (BMI), blood pressure (BP), hemoglobin A1c (HbA1c), high-density lipoprotein (HDL), low-density lipoprotein (LDL), left ventricle ejection fraction (LVEF), New York heart association (NYHA), chronic obstructive pulmonary disease (COPD)

**Table 2.**
*Description of missing values from ZOL Genk Hospital considering the mortality predictors in heart failure.*

| Parameter | Missing value (n) | Missing value (%) |
|---|---|---|
| Age | 0 | 0 |
| Sex | 0 | 0 |
| Weight | 110 | 30 |
| Length | 113 | 31 |
| BMI | 120 | 33 |
| Systolic BP | 111 | 30 |
| Diastolic BP | 111 | 30 |
| HbA1c | 209 | 57 |
| HDL | 158 | 43 |
| LDL | 162 | 44 |
| Triglycerides | 152 | 41 |
| NT-ProBNP | 281 | 77 |
| LVEF | 88 | 24 |
| Diastolic dysfunction | 199 | 54 |
| NYHA | 321 | 87 |
| In-hospital rehabilitation | 0 | 0 |
| Smoking habits | 18 | 5 |
| Comorbidities | 0 | 0 |
| Cardiac history | 0 | 0 |
| Device | 0 | 0 |

**Legend:** Amounts of missing values per parameter in numbers and percentages.
**Abbreviation:** Amounts of patients (n), percentages of patients (%) body mass index (BMI), blood pressure (BP), hemoglobin A1c (HbA1c), high-density lipoprotein (HDL), low-density lipoprotein (LDL), left ventricle ejection fraction (LVEF), New York heart association (NYHA).

**Table 3.**
*Univariate regression analysis considering the mortality predictors in heart failure patients from ZOL Genk.*

| Parameter | Estimate | Odds Ratio (CI 95%) | p-value |
|---|---|---|---|
| **Age (year)** | 0.031 | 1.03 (1.00 – 1.06) | 0.047** |
| Sex | | | |
| Female | -0.022 | 0.96 (0.53 – 1.74) | 0.887 |
| Male | | | |
| **Weight (kg)** | -0.019 | 0.98 (0.96 – 1.00) | 0.073* |
| **Length (cm)** | 0.001 | 1.00 (0.97 – 1.03) | 0.953 |
| **BMI (kg/cm$^2$)** | -0.056 | 0.95 (0.88 – 1.01) | 0.100* |
| **Systolic BP (mmHg)** | -0.016 | 0.98 (0.97 – 1.00) | 0.026** |
| **Diastolic BP (mmHg)** | -0.030 | 0.97 (0.95 – 0.99) | 0.008*** |
| **HbA1c (mmol/mol)** | -0.022 | 0.98 (0.94 – 1.02) | 0.279 |
| **HDL (mg/dL)** | -0.019 | 0.98 (0.96 – 1.01) | 0.124 |
| **LDL (mg/dL)** | -0.006 | 0.99 (0.98 – 1.00) | 0.268 |
| **Triglycerides** | 0.001 | 1.00 (1.00 – 1.00) | 0.922 |
| **NT-ProBNP** | -0.001 | 1.00 (1.00 – 1.00) | 0.959 |
| **LVEF** | | | |
| HFpEF | -0.024 | | 0.926 |
| HFmrEF | -0.422 | | 0.177 |
| HFrEF | 0.446 | | 0.062* |
| **Diastolic dysfunction** | | | |
| 1 | -0.414 | | 0.182 |
| 2 | -0.392 | | 0.250 |
| 3 | 0.806 | | 0.043** |
| 4 | / | | / |
| **NYHA** | | | |
| I | -8.514 | | 0.998 |
| II | 7.743 | | 0.996 |
| III | -8.514 | | 0.997 |
| IV | 9.284 | | 0.995 |
| **In hospital rehabilitation** | | | |
| Yes | -0.325 | 0.52 (0.18 – 1.52) | 0.235 |
| No | | | |
| **Smoking habits** | | | |
| Yes | -0.099 | | 0.751 |
| Stopped | 0.222 | | 0.318 |
| No | -0.123 | | 0.595 |
| **Diabetes type 2** | | | |
| Yes | 0.073 | 1.16 (0.65 – 2.06) | 0.620 |
| No | | | |
| **COPD** | | | |
| Yes | 0.090 | 1.20 (0.63 – 2. 28) | 0.585 |
| No | | | |
| **Renal insufficiency** | | | |
| Yes | 0.179 | 1.43 (0.78 – 2. 63) | 0.247 |

| | | | |
|---|---|---|---|
| No | | | |
| **Cancer** | | | |
| Yes | 0.317 | 1.89 (0.66 – 5.41) | 0.239 |
| No | | | |
| **Cardiac history** | | | |
| Yes | -0.358 | 0.49 (0.15 – 1.59) | 0.235 |
| No | | | |
| **Device** | | | |
| Yes | -0.205 | 0.66 (0.38 – 1.17) | 0.159 |
| No | | | |

**Legend:** Logistic regression results per variable
**Statistics:** Univariate logistic regression *** p-value < 0.99 (significance level 99%), ** p-value < 0.95 (significance level 95%), * p-value < 0.90 (significance level 90%)
**Abbreviation:** Confidence interval (CI), body mass index (BMI), blood pressure (BP), hemoglobin A1c (HbA1c), high-density lipoprotein (HDL), low-density lipoprotein (LDL), left ventricle ejection fraction (LVEF), New York heart association (NYHA), chronic obstructive pulmonary disease (COPD)

**Table 4.**
*Correlations of predictive parameters from patients in ZOL Genk.*

| | | Age | Weight | BMI | Systolic BP | Diastolic BP |
|---|---|---|---|---|---|---|
| Age | r | 1.000 | | | | |
| | p | < 0.001 | | | | |
| Weight | r | - 0.290 | 1.000 | | | |
| | p | < 0.001* | < 0.001 | | | |
| BMI | r | - 0.100 | 0.853 | 1.000 | | |
| | p | 0.120 | < 0.001* | < 0.001 | | |
| Systolic BP | r | 0.178 | 0.088 | 0.167 | 1.000 | |
| | p | 0.004* | 0.160 | 0.008* | < 0.001* | |
| Diastolic BP | r | - 0.101 | 0.208 | 0.193 | 0.496 | 1.000 |
| | p | 0.108 | 0.001* | 0.002* | < 0.001* | < 0.001 |

**Legend:** Correlation results from significant continues parameters.
**Statistics:** Pearson's correlation test (r, correlation coefficient) and correlation probability (p, p-value)
* p-value < 0.90 (significance level 90%).
**Abbreviations:** Body mass index (BMI), blood pressure (BP).

**Table 5.**
*Multivariate regression model considering mortality predictive parameters in patients with heart failure in ZOL Genk.*

| Parameter | Estimate | Odds ratio (CI 95%) | p-value |
|---|---|---|---|
| **Age** | 0.033 | 1.03 (0.97 – 1.10) | 0.277 |
| **Sex** | | | 0.636 |
| Female | 0.134 | 1.31 (0.43 – 3.95) | |
| Male | | | |
| **BMI** | -0.073 | 0.93 (0.81 – 1.06) | 0.264 |
| **Diastolic BP** | -0.045 | 0.96 (0.91 – 1.00) | 0.054* |
| **NT-proBNP** | 0.001 | 1.00 (0.99 – 1.00) | 0.624 |
| **LVEF** | | | 0.324 |
| HFpEF | 0.114 | - | |
| HFmrEF | -0.574 | - | |
| HFrEF | 0.460 | - | |
| **Diastolic dysfunction** | | | 0.373 |
| 1 | -0.517 | - | |
| 2 | -0.080 | - | |
| 3 | 0.597 | - | |
| 4 | - | - | |
| **In-hospital rehabilitation** | | | 0.959 |
| Yes | -0.019 | 0.96 (0.23 – 4.02) | |
| No | | | |
| **Diabetes type 2** | | | 0.188 |
| Yes | 0.348 | 2.01 (0.71 – 5.67) | |
| No | | | |
| **COPD** | | | 0.488 |
| Yes | 0.214 | 1.53 (0.48 – 5.05) | |
| No | | | |
| **Renal insufficiency** | | | 0.807 |
| Yes | -0.074 | 0.86 (0.26 – 2.85) | |
| No | | | |
| **Cancer** | | | 0.676 |
| Yes | 0.205 | 1.51 (0.23 – 9.90) | |
| No | | | |

**Legend:** Logistic regression model with significant independent parameters (age, BMI, diastolic BP and diastolic dysfunction) with control variables (sex and comorbidities: diabetes type 2, COPD, renal insufficiency and cancer)
**Statistics:** Multivariate logistic regression * p-value < 0.90 (significance level 90%)
**Abbreviations:** Confidence interval (CI), body mass index (BMI), blood pressure (BP), left ventricle ejection fraction (LVEF)

**Table 6.**
*Univariate logistic regression of significant predictive parameters for in-hospital rehabilitation in ZOL Genk.*

| Parameter | Estimate | Odds ratio (CI 95%) | p-value |
|---|---|---|---|
| Age | -0.048 | 0.95 (0.93 – 0.98) | 0.001*** |
| Systolic BP | -0.027 | 0.97 (0.96 – 0.99) | 0.003*** |
| Triglycerides | 0.004 | 1.00 (1.00 – 1.01) | 0.0418** |
| Smoking habits | | | |
| Stopped | 0.492 | - | 0.037** |

**Legend:** Predictive parameters for in-hospital rehabilitation.
**Statistics:** Univariate logistic regression *** p-value < 0.99 (significance level 99%), ** p-value < 0.95 (significance level 95%)
**Abbreviations:** Confidence interval (CI), blood pressure (BP)

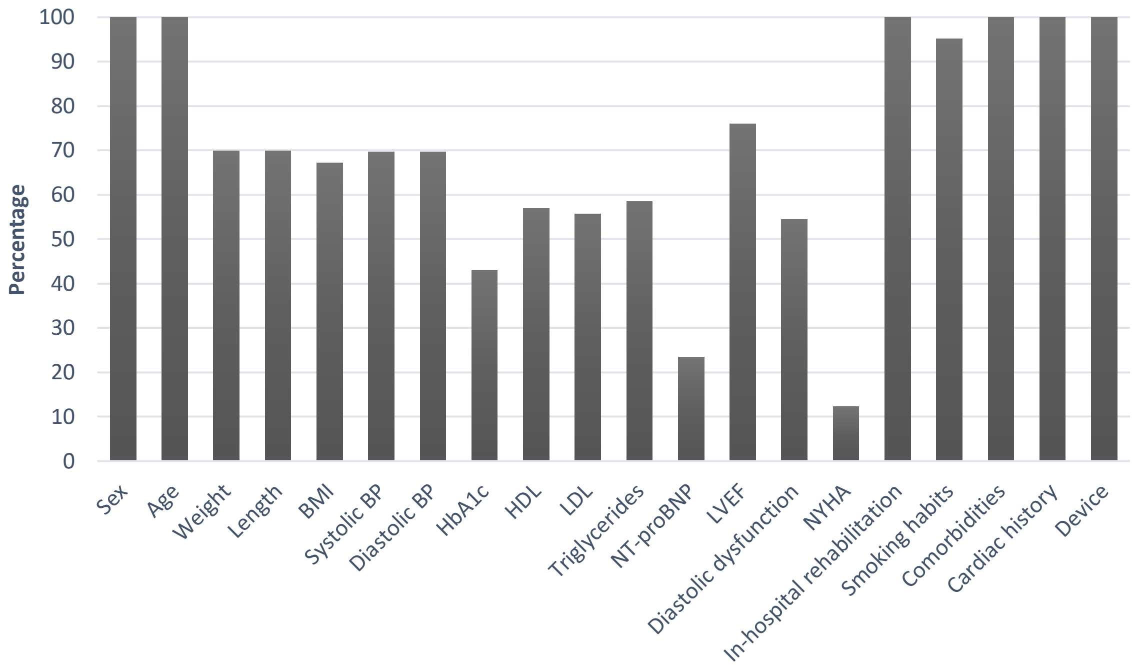


*Figure 1.* **Percentages of measured parameters from heart failure patients in ZOL Genk.**

www.uhasselt.be
Campus Hasselt | Martelarenlaan 42 | BE-3500 Hasselt
Campus Diepenbeek | Agoralaan gebouw D | BE-3590 Diepenbeek
T + 32(0)11 26 81 11 | E-mail: info@uhasselt.be

UHASSELT
KNOWLEDGE IN ACTION

# INVENTARISATIEFORMULIER WETENSCHAPPELIJKE STAGE DEEL 2

| DATUM | INHOUD OVERLEG | HANDTEKENINGEN |
|---|---|---|
| 22/10/2020 | Overleg ethische commissie | Promotor: dr. prof. Hansen D.<br>Copromotor/Begeleider: Verboven K.<br>Student(e): Iris Ivens<br>Student(e): Kathy Verreydt<br>student(e): Femke Tielemans<br>student(e): Minneke Verbeeck |
| 20/11/2020 | Bespreking praktische mogelijkheden retrospectief onderzoek | Promotor: dr. prof. Hansen D.<br>Copromotor/Begeleider: Verboven K., Mirte Stifter & Lore Jennen<br>Student(e): Iris Ivens<br>Student(e): Kathy Verreydt<br>student(e): Femke Tielemans<br>student(e): Minneke Verbeeck |
| 16/04/2021 | Bespreking wijziging masterproef topics adhv verzamelde data | Promotor: dr. prof. Hansen D.<br>Copromotor/Begeleider: Verboven K.<br>Student(e): Iris Ivens<br>Student(e): Kathy Verreydt<br>student(e): Femke Tielemans<br>student(e): Minneke Verbeeck |
| 23/04/2021 | Finale masterproef topic gekozen, data en statistiek besproken | Promotor: dr. prof. Hansen D.<br>Copromotor/Begeleider:<br>Student(e): Iris Ivens<br>Student(e): Kathy Verreydt<br>student(e): Femke Tielemans<br>student(e): Minneke Verbeeck |